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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/700,838

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EXAMINER

ROYDS, LESLIE A

ART UNIT

PAPER NUMBER

1614

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/700,838	<b>Applicant(s)</b> FIKSTAD ET AL.	
	<b>Examiner</b> Leslie A. Royds	<b>Art Unit</b> 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 28 April 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 35,51,52,54-61,65 and 75-82 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 35,51-52,54-61,65,75-82 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>28 April 2008</u> .   | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

**Claims 35, 51-52, 54-61, 65 and 75-82 are presented for examination.**

A request for continued examination under 37 C.F.R. 1.114, including the fee set forth in 37 C.F.R. 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R. 1.114, and the fee set forth in 37 C.F.R. 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 C.F.R. 1.114. Applicant's payment and submission filed April 28, 2008, has been received and entered into the present application. Accordingly, prosecution has been reopened.

Applicant's Information Disclosure Statement (IDS) submitted April 28, 2008 has also been received and entered into the present application. As reflected by the attached, completed copy of form PTO/SB/08A (one page total), the Examiner has considered the cited reference.

Claims 35, 51-52, 54-61, 65 and 75-82 remain pending and under examination. Claims 35 and 59-60 are amended. Claims 48-50 are cancelled.

Applicant's arguments, filed April 28, 2008, have been fully considered. Rejections and objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

#### ***Claim Rejections - 35 USC § 103 (New Grounds of Rejection)***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 35, 51-52, 54-61, 65 and 75-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amselem et al. (U.S. Patent No. 5,891,469; 1999) in view of The Merck Index (Eleventh Edition, Monograph 2277; 1989, p.353-354), each already of record.**

Amselem teaches pharmaceutical compositions capable of increasing the oral bioavailability of a lipophilic substance (col.5, 1.40-50), comprising: (1) a lipophilic substance that possesses low water solubility and poor oral bioavailability (col.1, 1.21-22), such as lipophilic substances that have a water solubility of less than 50 µg/ml (col.5, 1.43-47), e.g., cannabinoids (col.5, 1.44), which have aqueous solubility of a few micrograms or less, (2) the surfactant alpha-tocopherol polyethylene glycol succinate (also meets Applicant's limitation directed to "tocopherol succinate", see, e.g., present claims 42-43), usually with a mean molecular weight of 1000 (col.5, 1.49-66), and further (3) at least one dispersion adjuvant, such as tocopherol acetate, polyvinylpyrrolidone, a medium or long chain triglyceride and/or polyethylene glycol (col.6, 1.23-26 and col.6, 1.58-66). Amselem also teaches that the disclosed composition may be administered in a therapeutically effective amount to a mammal in need of such a substance (see claim 19; col.14), wherein the substance may be in a gelatin capsule or tablet unit dosage form (see claims 9-10; col.14) and may also comprise any suitable nontoxic carrier or diluent powder or additive (col.7, 1.4-15). Amselem further teaches that the lipophilic substance is present from 0.01-50% of the total solid weight of the composition, the surfactant TPGS is present from 5-65% of the total solid

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weight of the composition and the dispersion adjuvant is present from 5-75% of the total solid weight of the composition (col.6, l.37-57). Still further, Amselem demonstrates that pharmaceutical compositions prepared according to the disclosure of the reference are capable of release of the active drug over 120 minutes, which is equivalent to Applicant's "extended period of time" of 2 hours as instantly claimed (see, e.g., instant claims 35 and 59-60). Please see, e.g., Figure 1 of Amselem, which measured the percentage release of the active therapeutic agent (i.e., dexanabinol) over 120 minutes using various formulations prepared in accordance with the invention as disclosed. Note that, for several of the tested formulations, release of the active agent increased gradually over the course of 120 minutes (i.e., 2 hours) in the absence of a release plateau (see, e.g., Figure 1).

The teaching of tocopherol polyethyleneglycol (PEG) succinate in Amselem, especially tocopherol polyethyleneglycol 1000 succinate, as the surfactant component of the disclosed pharmaceutical composition places the use of either the racemic or either enantiomeric form (d- or l-) of tocopherol PEF succinate clearly within the possession of the public. Furthermore, though Amselem et al. does not expressly recognize the "release modulating" properties of the, e.g., tocopherol PEG succinate, tocopherol acetate, polyvinylpyrrolidone, or medium or long chain triglyceride, the very teaching of the identical chemical entity in overlapping amounts clearly indicates that whatever release modulating properties that Applicant has attributed to either of these compounds are necessarily present, absent factual evidence to the contrary, since chemical compounds cannot have mutually exclusive properties. Please reference MPEP §2112.01.

Amselem et al. fails to teach the use of cilostazol as the specific therapeutic drug of the instantly claimed pharmaceutical composition (claims 35 and 59-60) or the synchronized release of cilostazol and solubilizer with a correlation coefficient of greater than 0.80 (claims 51 and 75).

In view of the fact that Amselem et al. teaches the disclosed pharmaceutical compositions for formulating any of a variety of lipophilic substances, i.e., those with low water solubility and poor oral

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bioavailability, one of ordinary skill in the art at the time of the invention would have found it *prima facie* obvious to use such a delivery preparation for the formulation of other highly hydrophobic drugs (i.e., those with low water solubility and, thus, poor bioavailability), such as cilostazol, because, as The Merck Index teaches, this antithrombotic agent was well known in the art to be practically insoluble in water (see Monograph 2277). Accordingly, in view of the extensive hydrophobicity of the compounds taught by Amselem et al. and cilostazol, the skilled artisan would have had a reasonable expectation of success in effectively solubilizing cilostazol in the delivery vehicle disclosed by Amselem et al. because of the demonstrated success in effectively solubilizing the exemplary hydrophobic agents (i.e., dexanabinol, CoQ10, etc.) of the reference into such a formulation. Further, such a person would have been motivated to do so in order to enable effective dosing of cilostazol with concomitant enhancement of resorption and bioavailability levels, reduced variability in resorption and bioavailability levels and also a concomitant reduction in the amount required to achieve effective dosing.

With regard to present claims 51 and 75, which are directed to the synchronized release of cilostazol and solubilizer with a correlation coefficient of greater than 0.80, such correlation values are, absent factual evidence to the contrary, present in the reference because Amselem et al. teaches the formulation of the lipophilic drug with the surfactant and dispersion adjuvant compounds in clearly overlapping amounts and, thus, in the same ratios as presently claimed to produce a composition that is substantially the same as that presently claimed. In other words, the fact that Amselem et al. teaches identical components in identical, or at the very least, overlapping, amounts is clearly indicative of the fact that any release characteristics attributed to such a composition would be necessarily present in the prior art of Amselem et al., absent factual evidence to the contrary. Please see MPEP §2112.01[R-3] ("Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433

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(CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705,709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990)).

### ***Conclusion***

Rejection of claims 35, 51-52, 54-61, 65 and 75-82 is proper.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds/  
Patent Examiner, Art Unit 1614

July 17, 2008

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/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614